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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,402	02/11/2002	Marla Steinbeck	STE01-NP001	5286

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EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

4/C

Office Action Summary	Application No.	Applicant(s)	
	10/073,402	STEINBECK, MARLA	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 1/3/2005 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claims 7, 12-14 cancelled.
2. Claims 1-6, 8-11 are under examination.

Claim Rejections - 35 USC § 112

Enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The instant invention directs to a method of early diagnosing an inflammatory disease or condition associated with articular cartilage or bone surfaces in a mammal, comprising obtaining a patient's sample and detecting an amount of a chlorinated peptide(s) in said sample.

The core of the current invention lies on the correlation of the measurement of the amount of chlorinated peptides in a patient's sample to the association of the inflammatory condition of the cartilage or bone diseases. Nevertheless, applicant does not provide guidance, instructions or working example(s) sufficiently as to enable one skilled in the art to use the recited method for diagnosing the said inflammatory condition by determining the amount of the chlorinated compound/peptides in the patient's sample.

As pointed out by applicant, the current invention is to diagnose "[t]he presence of these compound/peptides in join fluid, serum and/or urine will serve as a useful clinical *marker* for inflammation associated with articular cartilage." (See page 39, line 4-6)(emphasis added). However, in light of specification, applicant merely presented a total of *4* patient's samples in concluding that the recited method can be used as a diagnosing tool for inflammatory cartilage disorder (See page 33, second paragraph; Table III; emphasis added). Page 33, Table III, applicant presented 4 patients' experimental samples, one "control" (#001, acute cruciate ligament), one early OA (#002) and two advanced osteoarthritis (# 003 and #004; OA). Out of the four samples, only one sample designated as "*early OA*" shows positive Cl-peptides (chlorinated peptide) signal under mass spectrum analysis (emphasis added). In particular, two other patients suffer the *similar OA* do not show the chlorinated peptide signal (emphasis added). Those data suffer inadequacy of interpretation at least for the following reasons.

First, both the early and the advanced OA suffer on the same targets, i.e. bone surface or cartilage, with different degrees of severity. However, applicant's data shows only patient 002 (early OA) can be positively detected (See Table III, page 32, line 28-32). The other two patients, suffering similar inflammatory disease or condition associated with articular cartilage or bone surfaces, cannot be detected. The recited method, i.e. detecting an amount of a chlorinated

compound/peptide(s) in patients, cannot be used to detect advanced OA which is also a inflammatory disease or condition associated with articular cartilage or bone surface.

Second, there is no "true" control sample, e.g. healthy individuals, conducted in the experiments as a comparison to the "early OA" or "advanced OA." Most importantly, there is only one patient's sample showing a positive chlorinated peptide signal compared to the rest of the three samples. Therefor, the current invention merely presents *ONE* experimental sample and intends to conclude to an association with inflammatory disease or condition (emphasis added). The only *one* experimental result is not sufficient to reflect a statistical reliable model without considering other factors, such as age or sex. Furthermore, there is no standard deviation to reflect the accuracy/or reliability of the experimentation since there is only one "early OA" patient in the test.

As a diagnostic marker for any disease, one artisan in the art would consider both specificity and sensitivity to preclude false positive and false negative results for accuracy. With respect to sensitivity, the invention cannot detect similar OA patients who also have inflammatory conditions associated with cartilage or bone surface. With respect to specificity, the lack of sufficient sample size in the current invention cannot be used to represent in a general population, i.e. a marker, for adequately diagnosing inflammatory diseases or condition associated with cartilage or bone surfaces.

In view of the aforementioned lack of predictability in the art, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in the applicant's specification of how to effectively practice the recited method and absent working examples.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-6, 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 1, line 1, "early diagnosis" is vague and indefinite. It is not clear what constitutes "early" with respect to time for the detection.

Response to Applicant's Arguments

Applicant submits an additional data (Table I in Exhibit A, 6 more samples compared to 4 samples in Table III) arguing that the "[t]his finding and conclusion is further supported and confirmed by the additional data produced by the inventors after filing the application" (See Remarks, page 2, second paragraph; Exhibit A). Applicant's arguments have been considered but are not persuasive.

The additional data compose of 4 categories, namely "Torn ACL"(acute crucial ligament), "Torn Meniscus" (tear in the shock-absorbing cartilage), "Early OA"(early osteoarthritis) and "advanced OA"(advanced osteoarthritis). In view of the newly submitted data, the results nevertheless still suffer insufficiency to support the recited claims for this invention.

First of all, there is no healthy control in the set of data. We do not know whether the chlorinated peptides would occur in a healthy people or not. The current invention does not direct to identify inflammatory early osteoarthritis among the similar cartilage diseases, such as "Torn ACL", "Torn Meniscus" or "Advanced OA". Rather applicant is claiming a method of diagnosing an inflammatory disease associated with articular cartilage or bone surface in a general population.

Second, most strikingly, sample 015 characterized as "Early OA" does not even show *any* chlorinated peptide (See Table I in Exhibit A)(emphasis added). If inventor claims the instant method is capable of diagnosing the early OA patients by detecting the *presence* of chlorinated peptides, the result in Table I is apparently contradict to what is claimed here (emphasis added).

Taken together, the newly submitted data, albeit with additional sample size (6 more), it nonetheless suffers both statistical and scientific insufficency. In view of the aforementioned lack of predictability in the art, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in the applicant's specification of how to effectively practice the recited method and absent working examples.

Conclusion

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

March 10, 2005

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
03/17/05